



OX513A *Aedes aegypti* control programme in the Cayman Islands

Expansion phase

For submission to the National Conservation Council, Cayman Islands -January 2017

Introduction

The Cayman Islands Mosquito Research and Control Unit (MRCU) has a longstanding collaborative relationship with UK based Oxitec Ltd. in the deployment of the OX513A technology as a tool to suppress *Aedes aegypti*, the mosquito that spreads Zika, dengue and chikungunya. Following successful experimental releases and suppression trials in 2009-2010 under permit from the Cayman Departments of Environment (DoE) and Agriculture (DoA), and the recent successful establishment of a small scale operational program in 2016 under DoE and DoA permission as approved by the National Conservation Council (NCC), the MRCU is seeking to expand the operational use of the OX513A tool in response to the most pressing MRCU operational needs across the Cayman Islands. The current production facility located in the MRCU compound has been servicing a populated area of approximately 2000 residents in West Bay and serves to establish the OX513A program as a valuable operational tool for the MRCU in its *Aedes aegypti* control efforts. Operational scale-up in Grand Cayman is proposed see the staged expansion of OX513A use across the entire island once additional production capacity is established. Scenarios for production scale up and program expansion are outlined within this document. Additionally, as *Aedes aegypti* control endpoints are realised in the currently permitted release area, additional production capacity of the currently installed Mobile Rearing Unit (MRU) can be utilized in response to the highest priority emerging threats posed by *Aedes aegypti* as identified by the MRCU. Currently there are two scenarios under consideration to ensure established OX513A production capacity is best utilized in 2017 while additional production capacity is being established. Beyond the currently permitted area in West Bay, scenarios for a modest expansion of the current treatment area in West Bay are under consideration, as well as using OX513A on the island of Cayman Brac in response to the recent detection of an established population of *Aedes aegypti* on that island. The identification of *Aedes aegypti* in Cayman Brac is illustrative of the need for flexibility in deploying the OX513A technology within the territory of the Cayman Islands as the MRCU undertake surveillance of *Aedes aegypti* populations and identify where the OX513A technology is best suited.

This document provides a general description of the programmatic use of OX513A and the operational approach to a staged expansion of the program across Grand Cayman and the Cayman Islands as needed, including the expansion of mosquito rearing facilities and expected production and release targets. The document is laid out in the following sections:

- A. General programme description- Adaptive management of OX513A releases
- B. Staged expansion of the OX513A programme
- C. Compliance oversight and reporting

A DoE permit application is supplied as Appendix 6 which requests approval for the importation of a set maximum number of OX513A eggs/month for program deployment as needed within the Cayman Islands accounting for eventual production scale-up. As appropriate, the permit application includes reference only to the previous permit application to avoid redundancy as

key information on the OX513A technology has previously been reviewed by the NCC under the current project approval.

A. General programme description- Adaptive management of OX513A releases

In a globally or regionally centralised egg production facility (e.g. currently UK based) OX513A eggs are continually produced from a cycling colony of homozygous OX513A and subject to regular quality control checks as established in Standard Operating Procedures (SOPs). OX513A eggs are shipped in regular shipments throughout the course of the program to the facility near the release site where they are reared through to pupae, sex sorted to select male pupae, the males are matured to adults for release. Sexually mature OX513A males are released from predefined release points generally following the road patterns in the release area to ensure even coverage of the area.

OX513A can be deployed both to suppress a local *Aedes aegypti* population, as well as maintain suppression and prevent population resurgence in an area with low levels of *Aedes aegypti*. Under the adaptive management model, release rates are dynamically adjusted in proportion to the local *Aedes aegypti* population as it responds to suppression through the release of OX513A self-limiting males, as well as fluctuations in response to seasonality and/or other controls used in the context of a broader Integrated Vector Management (IVM) approach.

The OX513A programme can be divided into three sequential phases:

1. Preparation Phase:

This Preparation Phase is used to conduct baseline mosquito population measures, establish production and distribution capacity, and finalise a release plan for the release area, including initial application rates and locations. The OX513A program is compatible with conventional control programs and exploiting synergy in an integrated approach with local vector control activities is evaluated in the preparation phase in addition to collating historical climatic, and vector surveillance and control data. Although the chosen number of OX513A males for releases is relative to the estimated size of the target *Aedes aegypti* population, wild populations of *Aedes aegypti* are most closely associated to human populations and therefore the release rate is often described as 'number of OX513A males per person'. It is during the preparation phase that community engagement activities are started.

2. Suppression Phase:

The Suppression Phase is when the *Aedes aegypti* population is initially brought under control. Ideally, this can be timed to take advantage of seasonally low pest pressures or as a follow-on from existing vector management activities.

Following the Preparation Phase, the initial releases of OX513A males take place in a systematic manner from pre-determined georeferenced release points at regular time intervals, for even and consistent coverage of the treatment area. Release points are generally spaced no more than 100m apart, and releases occur 3 to 7 times per week at a constant release rate. The initial release rate is a function of the human population and the estimated wild *Aedes aegypti* infestation level in the treatment area at start of releases. The rate of release is adapted on an ongoing basis as informed by data collected throughout the release, and is generally reduced as control of the wild *Aedes aegypti* population is achieved.

3. *Maintenance Phase:*

Once the *Aedes aegypti* population has been reduced to target levels the programme enters the Maintenance Phase, designed to prevent resurgence of the wild *Aedes aegypti* population. A range of approaches can be adopted and customised to individual control programmes. Re-infestation in this context may be caused by the immigration of wild *Aedes aegypti* into the programme area, perhaps as eggs or adults inadvertently moved by humans. It may also relate to the size of the egg bank (eggs laid at an earlier period remaining in the environment), though the viability of such eggs is expected to decline over time such that this is expected to be a source of re-infestation for a limited period only. This approach can be applied to contiguous sub-areas of the program as they become well controlled, even while other areas remain in the Intervention Phase. In the event that effective elimination of *Aedes aegypti* is achieved in Grand Cayman, the Maintenance phase focuses on monitoring activities island wide, and potential ongoing releases in ports of entry, or other areas identified by MRCU, which are areas of high risk for re-infestation.

Ongoing monitoring of the wild population pre, during and post release is undertaken using egg surveillance (ovitrapping). Supplementary adult trapping may be deployed during critical phases of program. Identification, detection, and trapping methodologies are all well defined in SOPs and are used to inform the adaptive management of OX513A releases.

B. Staged expansion of the OX513A programme

The current *Aedes aegypti* control programme is being conducted under permit from the Cayman Department of the Environment (DoE) and importation of *Aedes aegypti* strain OX513A eggs permitted by the Cayman Department of Agriculture (DoA). The coverage area of the current project as described in the current DoE permit is the “South Part of West Bay” in an area which comprises about 1800 inhabitants over 300 acres (it may be more accurate however to describe it as the West part of West Bay district- as represented in Figure 1). The current activities represent the first stage of an *Aedes aegypti* control program which is anticipated to roll-out over the entire island of Grand Cayman over an 18-24 month period once additional rearing capacity is established, and subject to final Government approval.

Currently permitted activities:

- The current DoE permit serves to permit the release of *Aedes aegypti* OX513A in the current program area and is valid from June 8th, 2016 to June 30th 2017 (Appendix 1).
- The current DoA permit for importation was issued for a variance in OX513A egg importation amount and is valid from November 10th, 2016 to June 10th, 2017 (Appendix 2). Importation of OX513A eggs prior to November 10th, 2016 was under DoA permit issued June 20th, 2016 (Appendix 3).
- The DoE additionally issued, November 10th, 2016, approval for a variance in described activities, whereby OX513A pupae contained within sealed release devices are permitted to be housed in the Mosquito Research and Control Unit (MRCU) insectary (Appendix 4).

As a prerequisite to the permits issued for the variance application for the DoA and DoE permits issued November 10th, 2016, an interim project report was supplied to the National Conservation Council (NCC) (Appendix 5) and a site visit was conducted October 12, 2016. A minimum of one additional report under the current permit is to be provided by July 2017.

This section presents a proposed staged approach for the continuation of program activities under the OX513A *Aedes aegypti* control programme beyond the inhabited areas described in the current DoE permit. Operational expansion of the *Aedes aegypti* control program across Grand Cayman is proposed, and additionally, in response to recent surveillance activities, the potential for an OX513A control program to be deployed in Cayman Brac in 2017 is under evaluation by the MRCU. Delivery of the OX513A *Aedes aegypti* control program is to be undertaken via a partnership between Oxitec and the MRCU. Oxitec will continue with maintenance activities until the program has been implemented Island-wide in Grand Cayman, which is anticipated to be completed by mid-late 2019. Once suppression targets have been achieved island wide, ongoing maintenance is foreseen to be delivered by the MRCU through targeted releases. *Aedes aegypti* OX513A is seen as a tool in an Integrated Vector Management (IVM) approach for *Aedes aegypti* management and as such, the MRCU will be working with Oxitec to establish parameters for OX513A program delivery in the IVM context moving forward.

Stage 1 below describes proposed activities to be undertaken beginning in 2017, and Stage 2 below describes proposed scale up of activities into 2018 and beyond.

Stage 1 – Targeted use of existing production capacity beginning in 2017

Options are under consideration which aim to continue using the existing facilities at full OX513A production capacity as control targets are achieved in the existing treatment area.

Option a) The existing production facility could support a modest expansion into adjacent areas in West Bay in 2017 as part of an island wide roll-out. Targeted releases at lower levels could continue in the existing West Bay treatment area as the program moves into an operational maintenance phase in that area, intended to maintain suppression of the local *Aedes aegypti* population.

Option b) Once control targets are achieved in the current West Bay site, or concurrent with maintenance phase activities at that site, the existing OX513A production capacity could be used to target an emerging threat of *Aedes aegypti* in Cayman Brac. Ongoing surveillance of the local *Aedes aegypti* in Cayman Brac will inform OX513A program deployment options in that area.

Option c) Targeted releases at lower levels could continue in the existing West Bay treatment area as the program moves into an operational maintenance phase in that area, intended to maintain suppression of the local *Aedes aegypti* population.

Having the flexibility in regulatory permitting in response to the *Aedes aegypti* population dynamics will ensure the MRCU can best deliver control activities with the OX513A program.

Facilities:

As a continuation of the currently permitted activities, the mobile production facility situated in MRCU compounds at 99 Red Gate Road, and additionally the insectary subsequently approved under the application for variance to the permit are proposed to be collectively used to deliver the proposed Stage 1 activities beyond the current permit. The facilities have been previously described in the DoE permit (Appendix 1) and in the application for variance (Appendix 4). Additionally, a site visit was conducted by several NCC members on October 12, 2016 as part of the variance application process.

Production:

As part of the Quality Management System (QMS) implemented in the OX513A *Aedes aegypti* control programme, Standard Operating Procedures (SOPs) are in place to ensure oversight on production through all stages of the program from the receipt of OX513A eggs from the UK to the release of OX513A males in the treatment area. The SOPs also serve to ensure traceability and chain of custody for all OX513A material handled in the course of program delivery. Records maintained as part of the QMS also ensure appropriate documentation of activities to demonstrate regulatory compliance for the current permitted activities, and will be adapted as production practices and facilities scale up to meet program delivery targets proposed activities. QMS records will remain an integral means to oversee and demonstrate regulatory compliance.

The anticipated production from the existing facilities at maximum capacity is not expected to exceed 700,000 OX513A adult males/week

Proposed treatment areas- options under consideration:

The current treatment area is represented in Figure 1, and release points have been documented to date and retained. Under the current project, a control area has been monitored to provide a comparator (see Figure 1).

As suppression targets are achieved in the current treatment area, OX513A male release numbers are aimed to be reduced based on the adaptive management design of the program, and the area will be considered to move into a maintenance phase at a reduced release rate.

Production capacity from the existing mobile rearing unit could then be used to treat the most at risk areas, depending on the status of the local *Aedes aegypti* population at the time.

One option currently under consideration is to expand current operations to areas immediately adjacent to the initial treatment area, and continue expansion as the original treatment area moves entirely into maintenance phase. Figure 1 provides an example of the scale of expansion which could be supported by the current production capacity in Stage 1. A second option for Stage 1 expansion is illustrated in Figure 2, whereby the populated areas of Cayman Brac undergo OX513A releases. Treatment of this area would be possible as one operation covering all populated areas, and due to the isolation and limited immigration potential is an ideal area for OX513A program deployment. The exact boundaries of the specific treatment areas and timing is dependent on the measurement of key parameters at the time, Figures 1 and 2 are intended only to provide a sense of scale, and area for potential expansion sites, specific boundaries are to be determined as Stage 1 expansion progresses as informed by adaptive management and ongoing data collection. Other viable options may arise in response to *Aedes aegypti* surveillance activities.

At the time of operational expansion, more precise identification of program boundaries will be made and communicated to the National Conservation Council via the Department of the Environment as a matter of routine reporting. At that time, community engagement consistent with past program activities will be continued and focused on the expansion area in advance of operational expansion. Community engagement activities may entail the use of male OX513A transported to various sites in mesh cages for use in demonstration activities as appropriate (Figure 4). During community engagement demonstrations, OX513A males are not intentionally released from cages, but are used to demonstrate that male mosquitoes do not bite when a human hand enters the cage through a mesh sleeve, which is otherwise kept knotted to prevent release. At the end of their use, the cages containing OX513A males are placed at -15 degrees Celsius or colder for more than 12 hours prior to disposal of the insect material.

Beyond 2017, under an operational programme, the current facility is anticipated to be in constant production as part of the staged island wide coverage of Grand Cayman. Section B outlines how additional OX513A production capacity is proposed to be added in Stage 2 of island wide expansion.

Figure 1. Potential extent of area for 2017 expansion in West Bay.

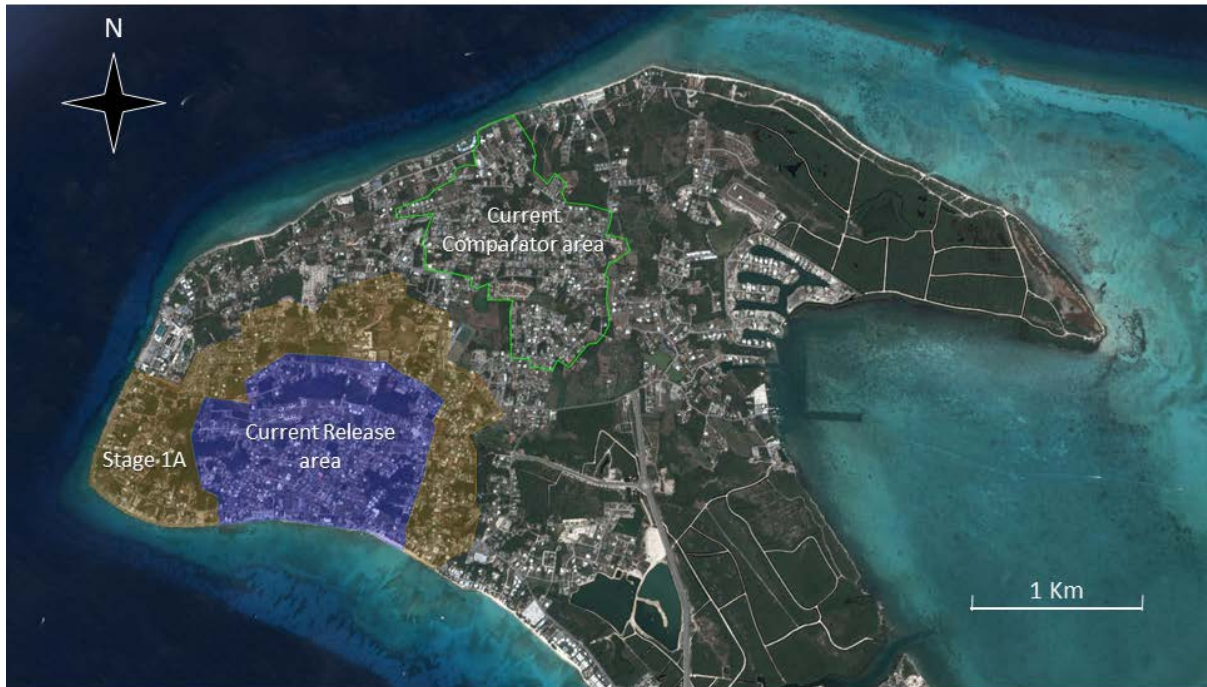


Figure 2. Potential extent of area for 2017 expansion in Cayman Brac



Stage 2 - Operational program scale up with expanded production capacity.

Stage 2 operational expansion proposes to roll out the OX513A *Aedes aegypti* program across inhabited areas of Grand Cayman over an 18-24 month period to achieve island wide control of *Aedes aegypti*. A formal agreement between Oxitec Cayman limited and the Government of the Cayman Islands is anticipated, to establish the main program activities and responsibilities for each party. An overview of the Stage 2 facility requirements, production activities, and the treatment area are provided below independent of the individual responsibilities of each party which will be established through contractual arrangements.

The Stage 2 program objectives are as follows:

- Establishment of additional rearing capacity for of OX513A on Grand Cayman.
- Significant suppression of the local population of *Aedes aegypti* throughout the island of Grand Cayman within 24 months of a date to be established in the final Heads of Agreement with MRCU.

Note: Effective elimination of *Aedes aegypti* from the island of Grand Cayman is a potential outcome, but not defined as a specific goal, although this may require a longer time-period than the initial 24-month duration of the Stage 2-Operations Phase.

Once island wide suppression targets are achieved, depending on the scenario to be agreed in the future, the existing facility is proposed to be under the operation of the MRCU, to deliver maintenance releases of OX513A, and in the treatment of any localised “hot-spots” and “entry-ports” of *Aedes aegypti* re-infestation.

Key elements of Stage 2 are presented below.

Facilities

The rearing facilities used in Stage 2 may be based either on a modular system using multiple adapted shipping containers, the numbers of which can be increased based on production needs, or the adaptation of a suitable permanent building structure, or a combination of the two. A final decision will be taken based on the most optimal production solution in light of any constraints identified in the planning process.

Oxitec mobile insectaries such as the existing mobile rearing unit (MRU) in place in the MRCU compound, 99 Red Gate Road are designed to Cayman Islands Building Codes and are based on standard 40-foot shipping containers structurally modified and fitted out under factory conditions. The laboratories are internally insulated and contain basic services such as water supply/extract, air conditioning and lighting.

The MRU currently in use in Grand Cayman is comprised of a single modified 40-foot shipping container. This MRU design can accommodate egg hatching, larval rearing and adult eclosion activities for male OX513A, as was done early in the current project, or be used solely for egg hatching and larval rearing, with adult male OX513A eclosion taking place in a separate insectary

building or adapted shipping container, as is now undertaken following the approval of a variance application for this activity. The Stage 2 operational expansion in Grand Cayman may be supported by the installation of additional production capacity based on a similar modular insectary design for all production activities whereby 40-foot shipping containers are either stand alone, or integrated together with appropriate allowance for passage of persons and services between. As with the current MRU design in use, appropriate ramp access as well as relevant occupational health and safety elements will be incorporated to ensure that the required Certificate of Occupancy can be issued by Cayman Islands Department of Planning.

Modular insectaries could be installed in a suitable location to be agreed contractually with the Cayman government at a future date. Installation will require a stable ground surface with adequate access to utilities and waste water services. Integral to the modular design is that the production modules can be removed once suppression targets have been achieved island wide and the program enters island wide maintenance phase. Rearing of OX513A to support maintenance phase activities beyond the Stage 2 expansion can be supplied from the existing mobile unit and MRCU insectary currently situated at 99 Red Gate Road.

Depending on the site availability, a production insectary based on a conventional building structure may be purpose built, or modifications may be made to an existing building as required in a suitable location with adequate access to utilities and water and waste water supply. The leasing of an empty warehouse and retrofitting for the anticipated duration of the project for example would suit this purpose.

Production

As described in Stage 1, Standard Operating Procedures (SOPs) are in place to ensure oversight on production through all stages of the program from the receipt of OX513A eggs from the distribution facility (e.g. currently the UK) to the release of OX513A males in the treatment area. In the context of the Stage 2 expansion, specific SOPs will be developed to adapt to the scale up of production as part of the Quality Management System (QMS).

The anticipated maximum production capacity required is not anticipated to exceed 10 million OX513A males/week under the most optimal production scenario during the 18-24 month program Stage 2 period.

Treatment area

Figure 3 is a conceptual representation of potential expansion staging through from initial Stage 1 expansion beginning 2017, through to Stage 2a and 2b operational expansion through 2018-2019, with Grand Cayman brought into an ongoing operational maintenance phase beyond late 2019. As with Stage 1 expansion, specific boundaries are to be determined as informed by adaptive management and ongoing data collection. Less densely populated areas towards the eastern side of the island would be spot treated in inhabited areas only, thus most of the interior of the eastern side of the island would not be subject to release.

Designated animal sanctuaries under the Cayman National Conservation Law

The areas of Meagre Bay Pond and Colliers Bay Pond are designated Animal Sanctuaries under Part 3, and described in Schedule 4 of the National Conservation Law (2014). For permits authorising activities in a protected area, such as designated animal sanctuaries, the Council must be satisfied that the activity is compatible with the relevant management plan for the protected area. Given that the neither Meagre Bay Pond, nor Colliers Bay Pond represent typical *Aedes aegypti* habitat, OX513A releases in those areas are not anticipated, and excluding the areas will not impact program delivery. Any inhabited areas adjacent to the protected areas, such as the cluster of houses to the southwest of Meagre Bay pond, which may partially fall within the legal boundaries of the protected area as described in Schedule 4 of the National Conservation Law, may be treated with alternative measures as part of the overall Integrated Vector Management (IVM) activities undertaken by the MRCU. Due to the small size and ease of treating these potential areas with alternative measures, this approach should simplify the administration and permitting of the island wide proposal for the OX513A program, as such an approximately 500 metre buffer around the protected areas will not be subject to release.

Figure 3. Conceptual representation of potential expansion staging for Island wide treatment of Grand Cayman. Protected animal reserves and 500 surrounding buffer zone are indicated in red.



Figure 4. Mesh cages to be used in community engagement activities using OX513A



C. Compliance oversight and reporting

C.1 – Compliance oversight

Continuity in record keeping serves as the principal means to demonstrate and ensure compliance with conditions under current Department of the Environment (DoE) and Department of Agriculture (DoA) permissions with consistency and transparency.

The Cayman Islands DoE and DoA have both issued permits under their respective legal authorities to allow the OX513A *Aedes aegypti* control program to proceed in Grand Cayman. November 10th 2016, variances on total import volumes, and the location of rearing activities were granted. Project permits have a duration to June 2017 and specific conditions are defined in each (Appendices 1-4). Activities to date have been conducted in compliance with all permit conditions, and records are maintained as part of the operational standard for the delivery of the OX513A *Aedes aegypti* control program.

Documentation requirements such as Standard Operating Procedures (SOP's) are integral to program administration and records maintained as part of the Quality Management System (QMS) can serve to demonstrate compliance oversight. The principles of traceability and chain of custody for all OX513A material handled in the course of program delivery will remain integral

to the maintenance and development of new SOPs under all production scenarios moving forward. An analysis of record keeping requirements under an expanded OX513A *Aedes aegypti* control program will be undertaken to ensure that compliance with any new permit conditions may be demonstrated to the DoE, DoA or the NCC as needed.

C.2 - Reporting

A report is required to be provided by July 30th, 2017 under the existing DoE permit, with an additional project conclusion report at a later date if necessary.

It is proposed that beyond the reporting July 30th, 2017, as program moves into Stage 1 and Stage 2 operational expansion, the MRCU and Oxitec provide an annual report to include but not limited to, a technical summary report including treated areas, a report of community engagement activities, a regulatory compliance report against permit conditions.

Attachments:

- Appendix 1- 2016 NCC release permit – signed
- Appendix 2 -2016 MRCU import permit - 1kg Additional
- Appendix 3-2016- MRCU Import Permit
- Appendix 4- 2016 MRCU-Oxitec Variance Nov 2016
- Appendix 5 - Interim report MRCU & Oxitec - Oct 2016
- Appendix 6- Cayman Islands - Alien Species Application Permit